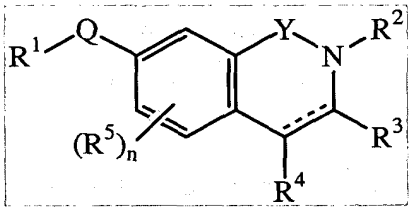
CLAIMS

What is claimed is:

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is independently selected from:

C_5 or C_6 cycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_5 or C_6 cycloalkyl-(C_1-C_8 alkylenyl);

C_8-C_{10} bicycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_8-C_{10} bicycloalkyl-(C_1-C_8 alkylenyl);

5- or 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobicycloalkyl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobicycloalkyl-(C_1-C_8 alkylenyl);

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5- or 6-membered heteroaryl;

Substituted 5- or 6-membered heteroaryl;

8- to 10-membered heterobiaryl;

Substituted 8- to 10-membered heterobiaryl;

R^2 is independently selected from:

H;

C_1-C_6 alkyl;

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Phenyl-O-(C_1-C_8 alkylenyl);

Substituted phenyl-O-(C_1-C_8 alkylenyl);

Phenyl-S-(C_1-C_8 alkylenyl);

Substituted phenyl-S-(C_1-C_8 alkylenyl);

Phenyl-S(O)-(C_1-C_8 alkylenyl);

Substituted phenyl-S(O)-(C_1-C_8 alkylenyl);

Phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

Substituted phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

Each substituted R^1 and R^2 group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C_1-C_6 alkyl;

CN;

CF_3;

HO;

(C_1-C_6 alkyl)-O;

(C_1-C_6 alkyl)-$S(O)_2$;

H_2N;

(C_1-C_6 alkyl)-N(H);

$(C_1\text{-}C_6\ \text{alkyl})_2\text{-N}$;

$(C_1\text{-}C_6\ \text{alkyl})\text{-C(O)O-}(C_1\text{-}C_8\ \text{alkylenyl})_m$;

$(C_1\text{-}C_6\ \text{alkyl})\text{-C(O)O-(1- to 8-membered heteroalkylenyl)}_m$;

$(C_1\text{-}C_6\ \text{alkyl})\text{-C(O)N(H)-}(C_1\text{-}C_8\ \text{alkylenyl})_m$;

$(C_1\text{-}C_6\ \text{alkyl})\text{-C(O)N(H)-(1- to 8-membered heteroalkylenyl)}_m$;

$H_2NS(O)_2\text{-}(C_1\text{-}C_8\ \text{alkylenyl})$;

$(C_1\text{-}C_6\ \text{alkyl})\text{-N(H)S(O)}_2\text{-}(C_1\text{-}C_8\ \text{alkylenyl})_m$;

$(C_1\text{-}C_6\ \text{alkyl})_2\text{-NS(O)}_2\text{-}(C_1\text{-}C_8\ \text{alkylenyl})_m$;

3- to 6-membered heterocycloalkyl-$(G)_m$;

Substituted 3- to 6-membered heterocycloalkyl-$(G)_m$;

5- or 6-membered heteroaryl-$(G)_m$;

Substituted 5- or 6-membered heteroaryl-$(G)_m$;

3- to 6-membered heterocycloalkyl-$(C_1\text{-}C_8\ \text{alkylenyl})_m\text{-}(G)_m$;

Substituted 3- to 6-membered heterocycloalkyl-$(C_1\text{-}C_8\ \text{alkylenyl})_m\text{-}(G)_m$;

5- or 6-membered heteroaryl-$(C_1\text{-}C_8\ \text{alkylenyl})_m\text{-}(G)_m$;

Substituted 5- or 6-membered heteroaryl-$(C_1\text{-}C_8\ \text{alkylenyl})_m\text{-}(G)_m$;

Phenyl-$(C_1\text{-}C_8\ \text{alkylenyl})_m\text{-}(G)_m$;

Substituted phenyl-$(C_1\text{-}C_8\ \text{alkylenyl})_m\text{-}(G)_m$;

Phenyl-$(G)_m\text{-}C_1\text{-}C_8\ \text{alkylenyl})_m$;

Substituted phenyl-$(G)_m\text{-}C_1\text{-}C_8\ \text{alkylenyl})_m$;

$(C_1\text{-}C_6\ \text{alkyl})\text{-S(O)}_2\text{-N(H)-C(O)-}(C_1\text{-}C_8\ \text{alkylenyl})_m$; and

$(C_1\text{-}C_6\ \text{alkyl})\text{-C(O)-N(H)-S(O)}_2\text{-}(C_1\text{-}C_8\ \text{alkylenyl})_m$;

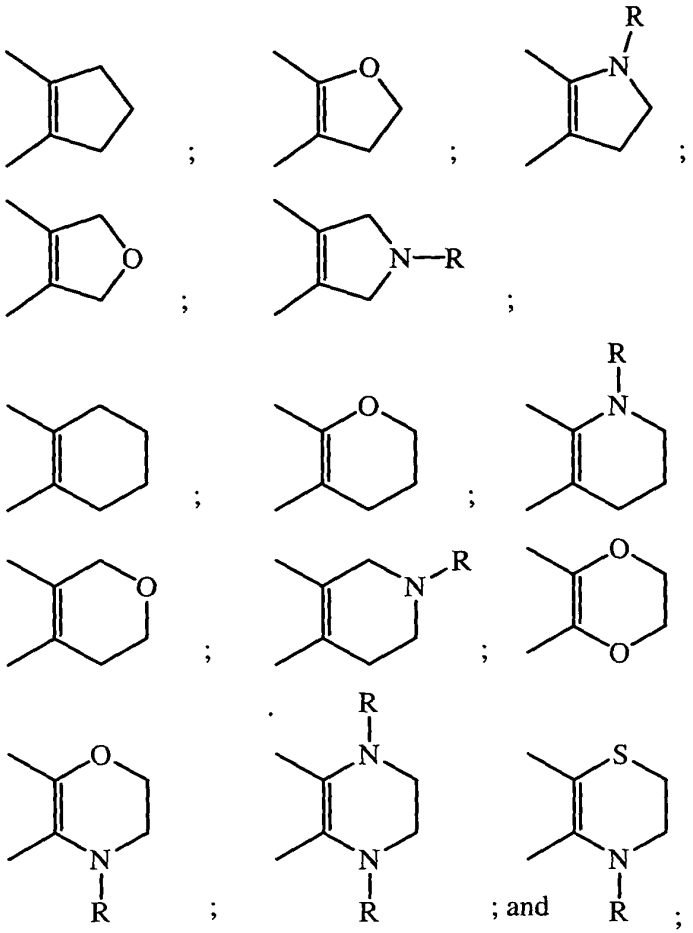
wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO_2C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



R is H or C_1-C_6 alkyl;

G is CH_2; C(=O)-N(H), N(H)-C(=O), C(=O)-O, O-C(=O), O, S, S(O); or $S(O)_2$;

Each m is an integer of 0 or 1;

R^3 and R^4 are independently selected from the groups:

H;

C_1-C_6 alkyl;

Substituted C_1-C_6 alkyl;

C_2-C_6 alkenyl;

Substituted C_2-C_6 alkenyl;

C_2-C_6 alkynyl;

Substituted C_2-C_6 alkynyl;

C_3-C_6 cycloalkyl;

Substituted C_3-C_6 cycloalkyl;

C_3-C_6 cycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_3-C_6 cycloalkyl-(C_1-C_8 alkylenyl);

Phenyl;

Substituted phenyl;

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl;

Substituted Naphthyl;

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

3- to 6-membered heterocycloalkyl;

Substituted 3- to 6-membered heterocycloalkyl;

3- to 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

Substituted 3- to 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl)

HO;

(C_1-C_6 alkyl)-O;

H_2N;

(C_1-C_6 alkyl)-N(H);

(C_1-C_6 alkyl)$_2$-N;

Each substituted R^3 and R^4 group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

H_2N;

C_1-C_6 alkyl;

CN;

CF_3;

(C_1-C_6 alkyl)-OC(O);

HO;

(C_1-C_6 alkyl)-O;

HS; and

(C_1-C_6 alkyl)-S;

wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO_2C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

R^5 is H, C_1-C_6 alkyl, H_2N, HO, or halo;

n is an integer of from 0 to 3;

Q is selected from:

OC(O);

$CH(R^6)C(O)$;

$OC(NR^6)$;

$CH(R^6)C(NR^6)$;

$N(R^6)C(O)$;

$N(R^6)C(S)$;

$N(R^6)C(NR^6)$;

$N(R^6)CH_2$;

SC(O);

$CH(R^6)C(S)$;

$SC(NR^6)$;

trans-(H)C=C(H);

cis-(H)C=C(H);

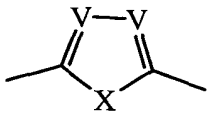
C≡C;

$CH_2C{\equiv}C$;

$C{\equiv}CCH_2$;

$CF_2C{\equiv}C$; and

$C{\equiv}CCF_2$;



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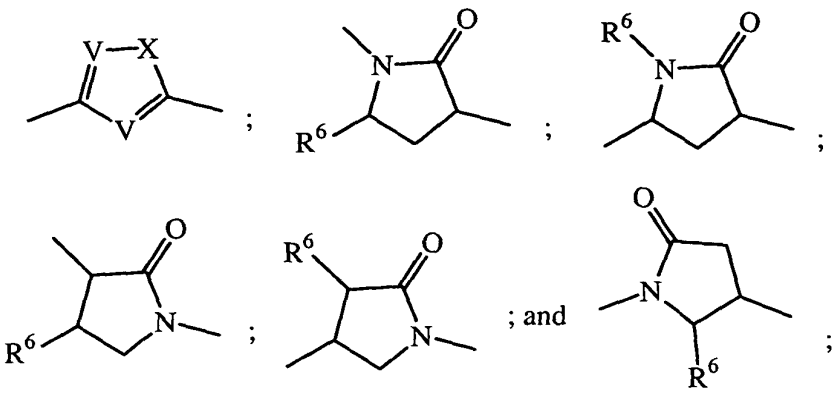


X is O, S, N(H), or N(C_1-C_6 alkyl);

Each V is independently C(H) or N;

R^6 is H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

Y is C(=O), CH_2; C(H)(R^7), C(R^7)$_2$; O; S; S(O); or S(O)$_2$;

Each R^7 is independently C_1-C_6 alkyl, H_2N; HO; or halo;

---- means a bond which is optionally present or absent;

wherein each C_8-C_{10} bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)$_2$, 1 N, 4 N(H), and 4 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)$_2$, 1 N, 4 N(H), and 4 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one

S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C_1-C_6 alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C_1-C_6 alkyl)$_2$-N group, the C_1-C_6 alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl;

wherein each group and each substituent recited above is independently selected; and

wherein the compound named 4-[1-oxo-7-(3-[1,2,3]triazol-1-ylprop-1-ynyl)-1H-isoquinolin-2-ylmethyl]benzoic acid is excluded.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y is C(=O), Q is N(R^6)C(O), n is 0, and R^3 and R^4 are independently H or CH_3.

3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y is C(=O), Q is C≡C, n is 0, and R^3 and R^4 are independently H or CH_3.

4. The compound according to any one of Claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein each of R^1 and R^2 are independently selected from:

Phenyl-(C_1-C_8 alkylenyl); and

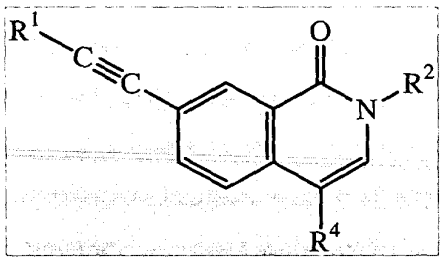
Substituted phenyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl); and

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

wherein each group and each substituent is independently selected.

5. The compound according to Claim 1 of Formula IIa



IIa

or a pharmaceutically acceptable salt thereof,

wherein the compound named 4-[1-oxo-7-(3-[1,2,3]triazol-1-ylprop-1-ynyl)-1H-isoquinolin-2-ylmethyl]benzoic acid is excluded.

6. The compound according to Claim 5, selected from the group:

4-[1-Oxo-7-(3-phenyl-prop-1-ynyl)-1H-isoquinolin-2-ylmethyl]-benzoic acid;

4-[4-Methyl-1-oxo-7-(3-phenyl-prop-1-ynyl)-1H-isoquinolin-2-ylmethyl]-benzoic acid;

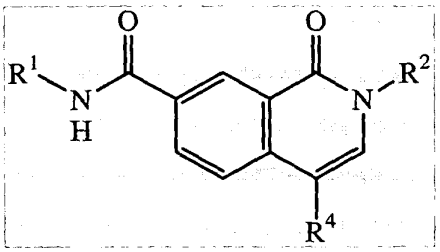
7-(3-Phenyl-prop-1-ynyl)-2-[4-(2H-tetrazol-5-yl)-benzyl]-2H-isoquinolin-1-one;

4-[1-Oxo-7-(3-phenyl-prop-1-ynyl)-1H-isoquinolin-2-ylmethyl]-N-piperidin-1-yl-benzamide; and

N-(5-Oxo-4,5-dihydro-1H-pyrazol-3-yl)-4-[1-oxo-7-(3-phenyl-prop-1-ynyl)-1H-isoquinolin-2-ylmethyl]-benzamide; or

a pharmaceutically acceptable salt thereof.

7. The compound according to Claim 1 of Formula III



III

or a pharmaceutically acceptable salt thereof.

8. The compound according to Claim 7, selected from the group:

1-Oxo-2-[4-(2H-tetrazol-5-yl)-benzyl]-1,2-dihydro-isoquinoline-7-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

4-{7-[(2-Methoxy-pyridin-4-ylmethyl)-carbamoyl]-1-oxo-1H-isoquinolin-2-ylmethyl}-benzoic acid;

1-Oxo-2-[4-(2H-tetrazol-5-yl)-benzyl]-1,2-dihydro-isoquinoline-7-carboxylic acid 4-methoxy-benzylamide;

1-Oxo-2-[4-(2H-tetrazol-5-yl)-benzyl]-1,2-dihydro-isoquinoline-7-carboxylic acid 3-methoxy-benzylamide;

1-Oxo-2-[4-(2H-tetrazol-5-yl)-benzyl]-1,2-dihydro-isoquinoline-7-carboxylic acid 4-methylsulfanyl-benzylamide; and

1-Oxo-2-[4-(2H-tetrazol-5-yl)-benzyl]-1,2-dihydro-isoquinoline-7-carboxylic acid (pyridin-4-ylmethyl)-amide; or

a pharmaceutically acceptable salt thereof.

9. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

10. The pharmaceutical composition according to Claim 9, comprising a compound according to Claim 8, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

11. A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from an osteoarthritis or rheumatoid arthritis

disease a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

12. The method according to Claim 11, wherein the compound administered is a compound according to Claim 8, or a pharmaceutically acceptable salt thereof.